

AMENDMENTS

IN THE CLAIMS:

~~Please cancel Claims 54-123 and 125-131, which have been withdrawn from consideration, without prejudice. Please cancel Claims 138, 144, 154, 161 and 162 without prejudice.~~

Please amend the claims as follows:

124. (Three Times Amended) A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding an OB polypeptide under conditions that provide for expression of the OB polypeptide *in vivo*, such OB polypeptide capable of modulating body weight and selected from the group consisting of:

- a) the amino acid sequence set out in SEQ ID NO: 2;
- b) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 2;
- c) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 2,

having an N-terminal methionine or an N-terminal polyhistidine;

- d) [c)] the amino acid sequence set out in SEQ ID NO: 4; [and]
- e)[d)] the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 4;

and

- f) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 4,

having an N-terminal methionine or an N-terminal polyhistidine.

[d) variants, including allelic variants, analogs and fragments of any of subparts (a) through (d), capable of modulating body weight.]

132. (Twice Amended) A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding a OB polypeptide [variant] under conditions that provide for expression of the OB [variant] polypeptide *in vivo*, such OB polypeptide [variant] capable of modulating body weight and selected from the group consisting of:

- a) the amino acid sequence set out in SEQ ID NO: 5;

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b) the amino acid sequence set out in amino acids 22-166 of SEQ ID NO: 5;
c) the amino acid sequence set out in amino acids 22-166 of SEQ ID NO: 5,
having an N-terminal methionine or an N-terminal polyhistidine;
d)[c)] the amino acid sequence set out in SEQ ID NO: 6; [and]
e)[d)] the amino acid sequence set out in amino acids 22-166 of SEQ ID NO: 6;
and
f) the amino acid sequence set out in amino acids 22-166 of SEQ ID NO: 6,
having an N-terminal methionine or an N-terminal polyhistidine.

133. (Twice Amended) A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding an OB polypeptide under conditions that provide for expression of the OB polypeptide *in vivo*, such OB polypeptide capable of modulating body weight wherein such [said] OB polypeptide has 83 percent or more amino acid [sequence] identity to the OB polypeptide amino acid sequence set out in SEQ ID NOS: 2, 4, 5, [or] 6, 23 or 25.

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134. (Twice Amended) A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding an analog [variant] of an OB polypeptide under conditions that provide for expression of the OB polypeptide analog *in vivo*, such OB polypeptide analog capable of modulating body weight and comprising amino acids 22-167 of SEQ ID NO:4 wherein one or more amino acids selected from the group consisting of amino acids 53, 56, 71, 85, 89, 92, 95, 98, 110, 118, 121, 122, 126, 127, 128, 129, 132, 139, 157, 159, 163 and 166 is substituted with another amino acid.

135. (Twice Amended) A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding an analog [variant] of an OB polypeptide under conditions that provide for expression of the OB polypeptide analog *in vivo*, such OB polypeptide analog capable of modulating body weight and comprising amino acids 22-166[7] of SEQ ID NO:6 wherein one or more amino acids selected from the group consisting of amino acids 52, 55, 70, 84, 88, 91, 94, 97, 109, 117, 120, 121, 125,

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126, 127, 128, 131, 138, 156, 158, 162 and 165 is substituted with another amino acid.

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136. (Amended) A method according to claim 163 [124] wherein said mammal is a mouse.

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137. (Amended) A method according to claim 163 [124] wherein said mammal is a human.

139. (Twice Amended) A method of delivering DNA encoding an OB polypeptide capable of modulating body weight to a mammal comprising administering to said mammal a vector which comprises such OB encoding DNA operatively associated with an expression control sequence, under conditions that provide for the expression of the OB polypeptide by the mammal [according to claim 138] wherein said OB polypeptide is selected from the group consisting of:

- a) the amino acid sequence set out in SEQ ID NO: 2;
- b) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 2;
- c) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 2,

having an N-terminal methionine or an N-terminal polyhistidine;

- d)[c)] the amino acid sequence set out in SEQ ID NO: 4;

- e)[d)] the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 4;

and

- f) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 4,

having an N-terminal methionine or an N-terminal polyhistidine.

- [e) variants, including allelic variants, analogs and fragments of any of subparts (a) through (d), capable of modulating body weight.]

140. (Twice Amended) A method of delivering DNA encoding an OB polypeptide capable of modulating body weight to a mammal comprising administering to said mammal a vector which comprises such OB encoding DNA operatively associated with an expression control sequence, under conditions that provide for the expression of the OB polypeptide by the

mammal [according to claim 138] wherein said [mammalian] OB polypeptide is [a variant] selected from the group consisting of the amino acid sequence set forth in:

- a) SEQ ID NO: 5;
- b) amino acids 22-166 of SEQ ID NO: 5;
- c) amino acids 22-166 of SEQ ID NO: 5, having an N-terminal methionine or an N-terminal polyhistidine;
- d)[c)] SEQ ID NO: 6; [and]
- e)[d)] amino acids 22-166 of SEQ ID NO: 6; and
- f) amino acids 22-166 of SEQ ID NO: 6, having an N-terminal methionine or an N-terminal polyhistidine.

141. (Twice Amended) A method of delivering DNA encoding an OB polypeptide capable of modulating body weight to a mammal comprising administering to said mammal a vector which comprises such OB encoding DNA operatively associated with an expression control sequence, under conditions that provide for expression of the OB polypeptide by the mammal, wherein said OB polypeptide has 83 percent or greater amino acid [sequence] identity to the OB polypeptide amino acid sequence set out in SEQ ID NOS: 2, 4, 5, [or] 6, 23 or 25.

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142. (Twice Amended) A method of delivering DNA encoding an analog of an OB polypeptide capable of modulating body weight to a mammal comprising administering to said mammal a vector which comprises such OB encoding DNA operatively associated with an expression control sequence, under conditions that provide for expression of the OB polypeptide analog by the mammal, [wherein] said OB polypeptide analog comprising[es] amino acids 22-167 of SEQ ID NO:4 wherein one or more amino acids selected from the group consisting of amino acids 53, 56, 71, 85, 89, 92, 95, 98, 110, 118, 121, 122, 126, 127, 128, 129, 132, 139, 157, 159, 163 and 166 is substituted with another amino acid.

143. (Twice Amended) A method of delivering DNA encoding an analog of an OB polypeptide capable of modulating body weight to a mammal comprising administering to said mammal a vector which comprises such OB encoding DNA operatively associated with an

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expression control sequence, under conditions that provide for expression of the OB polypeptide analog by the mammal, [wherein] said OB polypeptide analog comprising[es] amino acids 22-166[7] of SEQ ID NO:6 wherein one or more amino acids selected from the group consisting of amino acids 52, 55, 70, 84, 88, 91, 94, 97, 109, 117, 120, 121, 125, 126, 127, 128, 131, 138, 156, 158, 162 and 165 is substituted with another amino acid.

145. (Twice Amended) A method of expressing an OB polypeptide in a mammal comprising administering to said mammal a DNA vector which vector comprises DNA encoding an OB polypeptide capable of modulating body weight operatively associated with an expression control sequence [according to claim 144] wherein said OB polypeptide is selected from the group consisting of:

- a) the amino acid sequence set out in SEQ ID NO: 2;
- b) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 2;
- c) the amino acid sequence set out in amino acids 22-167 of SEQ ID NO: 2, having an N-terminal methionine or an N-terminal polyhistidine;
 - d)[c)] the amino acid sequence set out in SEQ ID NO: 4;
 - e)[d)] the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 4;

and

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f) the amino acid sequence set out in amino acids 22-167 of SEQ ID NO: 4, having an N-terminal methionine or an N-terminal polyhistidine.
[g) variants, including allelic variants, analogs and fragments of any of subparts (a) through (d), capable of modulating body weight.]

146. (Twice Amended) A method of expressing an OB polypeptide in a mammal comprising administering to said mammal a DNA vector which vector comprises DNA encoding an OB polypeptide capable of modulating body weight operatively associated with an expression control sequence [according to claim 144] wherein said [mammalian] OB polypeptide is [a variant] selected from the group consisting of the amino acid sequence set forth in:

- a) SEQ ID NO: 5;
- b) amino acids 22-166 of SEQ ID NO: 5;

c) amino acids 22-166 of SEQ ID NO:5, having an N-terminal methionine or an N-terminal polyhistidine;

d)[c)] SEQ ID NO: 6; [and]

e)[d)] amino acids 22-166 of SEQ ID NO: 6; and

f) amino acids 22-166 of SEQ ID NO:6, having an N-terminal methionine or an N-terminal polyhistidine.

147. (Twice Amended) A method of expressing an OB polypeptide in a mammal comprising administering to said mammal a DNA vector which vector comprises DNA encoding an OB polypeptide capable of modulating body weight operatively associated with an expression control sequence wherein said OB polypeptide has 83 percent or greater amino acid [sequence] identity to the OB polypeptide amino acid sequence set out in SEQ ID NOS: 2, 4, 5, [or] 6, 23 or 25.

148. (Twice Amended) A method of expressing an analog of an OB polypeptide in a mammal comprising administering to said mammal a DNA vector which vector comprises DNA encoding an OB polypeptide analog capable of modulating body weight operatively associated with an expression control sequence, [wherein] said OB polypeptide analog comprising[es] amino acids 22-167 of SEQ ID NO:4 wherein one or more amino acids selected from the group consisting of amino acids 53, 56, 71, 85, 89, 92, 95, 98, 110, 118, 121, 122, 126, 127, 128, 129, 132, 139, 157, 159, 163 and 166 is substituted with another amino acid.

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149. (Twice Amended) A method of expressing an analog of an OB polypeptide in a mammal comprising administering to said mammal a DNA vector which vector comprises DNA encoding an OB polypeptide analog capable of modulating body weight operatively associated with an expression control sequence, [wherein] said OB polypeptide analog comprising[es] amino acids 22-166[7] of SEQ ID NO:6 wherein one or more amino acids selected from the group consisting of amino acids 52, 55, 70, 84, 88, 91, 94, 97, 109, 117, 120, 121, 125, 126, 127, 128, 131, 138, 156, 158, 162 and 165 is substituted with another amino acid.

155. (Twice Amended) A method of expressing an OB polypeptide in a mammal comprising administering to said mammal a mammalian cell comprising an expression vector which vector comprises DNA encoding an OB polypeptide capable of modulating body weight operatively associated with an expression control sequence under conditions that provide for expression of the OB polypeptide by the mammal [according to claim 154] wherein said OB polypeptide is selected from the group consisting of:

- a) the amino acid sequence set out in SEQ ID NO: 2;
- b) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 2;
- c) the amino acid sequence set out in amino acids 22-167 of SEQ ID NO: 2,

having an N-terminal methionine or an N-terminal polyhistidine;

- d)[c)] the amino acid sequence set out in SEQ ID NO: 4;
- e)[d)] the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 4;
and
- f) the amino acid sequence set out in amino acids 22-167 of SEQ ID NO: 4,

having an N-terminal methionine or an N-terminal polyhistidine.

[e) variants, including allelic variants, analogs and fragments of any of subparts (a) through (d), capable of modulating body weight.]

156. (Twice Amended) A method of expressing an OB polypeptide in a mammal comprising administering to said mammal a mammalian cell comprising an expression vector which vector comprises DNA encoding an OB polypeptide capable of modulating body weight operatively associated with an expression control sequence under conditions that provide for expression of the OB polypeptide by the mammal [according to claim 154] wherein said [mammalian] OB polypeptide is [a variant] selected from the group consisting of the amino acid sequence set forth in:

- a) SEQ ID NO: 5;
- b) amino acids 22-166 of SEQ ID NO: 5;
- c) amino acids 22-166 of SEQ ID NO: 5, having an N-terminal methionine or an N-terminal polyhistidine;

- d)[c)] SEQ ID NO: 6; [and]

e)[d]) amino acids 22-166 of SEQ ID NO: 6; and
f) amino acids 22-166 of SEQ ID NO: 6, having an N-terminal methionine or an N-terminal polyhistidine.

157. (Twice Amended) A method of expressing an OB polypeptide in a mammal comprising administering to said mammal a mammalian cell comprising an expression vector which vector comprises DNA encoding an OB polypeptide capable of modulating body weight operatively associated with an expression control sequence[,] under conditions that provide for expression of the OB polypeptide by the mammal wherein said OB polypeptide has 83 percent or greater amino acid [sequence] identity to the OB polypeptide amino acid sequence set out in SEQ ID NOS: 2, 4, 5, [or] 6, 23 or 25.

158. (Twice Amended) A method of expressing an analog of an OB polypeptide in a mammal comprising administering to said mammal a mammalian cell comprising an expression vector which vector comprises DNA encoding an OB polypeptide analog capable of modulating body weight operatively associated with an expression control sequence, under conditions that provide for expression of the OB polypeptide analog by the mammal, [wherein] said OB polypeptide analog comprising[es] amino acids 22-167 of SEQ ID NO:4 wherein one or more amino acids selected from the group consisting of amino acids 53, 56, 71, 85, 89, 92, 95, 98, 110, 118, 121, 122, 126, 127, 128, 129, 132, 139, 157, 159, 163 and 166 is substituted with another amino acid.

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159. (Twice Amended) A method of expressing an analog of an OB polypeptide in a mammal comprising administering to said mammal a mammalian cell comprising an expression vector which vector comprises DNA encoding an OB polypeptide analog capable of modulating body weight operatively associated with an expression control sequence, under conditions that provide for expression of the OB polypeptide analog by the mammal, [wherein] said OB polypeptide analog comprising[es] amino acids 22-166[7] of SEQ ID NO:6 wherein one or more of amino acids selected from the group consisting of amino acids 52, 55, 70, 84, 88, 91, 94, 97, 109, 117, 120, 121, 125, 126, 127, 128, 131, 138, 156, 158, 162 and 165 is substituted with

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another amino acid.

Please add the following Claims:

-- 165. A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding an OB polypeptide analog under conditions that provide for expression of the polypeptide analog *in vivo*, said analog, capable of modulating body weight, comprising amino acids 22-167 of SEQ ID NOS: 2 or 4 wherein said analog is selected from the group consisting of polypeptides wherein:

- (a) the serine residue at position 53 is substituted with glycine, alanine, valine, cysteine, methionine, or threonine;
- (b) the serine residue at position 98 is substituted with glycine, alanine, valine, cysteine, methionine, or threonine; and
- (c) the arginine residue at position number 92 is substituted with asparagine, lysine, histidine, glutamine, glutamic acid, aspartic acid, serine, threonine, methionine, or cysteine.

166. A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding an OB polypeptide analog under conditions that provide for expression of the polypeptide analog *in vivo*, said analog, capable of modulating body weight, comprising an amino acid sequence of SEQ ID NOS: 2 or 4, wherein said analog is selected from the group consisting of polypeptides wherein:

- (a) one or more aspartic acid residues is substituted with glutamic acid;
- (b) one or more isoleucine residues is substituted with leucine;
- (c) one or more glycine or valine residues is substituted with alanine;
- (d) one or more arginine residues is substituted with histidine;
- (e) one or more tyrosine or phenylalanine residues is substituted with tryptophan;
- (f) one or more of residues 121 through 128 is substituted with glycine or alanine; and
- (g) one or more residues at positions 54 through 60 or 118 through 166 is

substituted with lysine, glutamic acid, cysteine, or proline.

167. A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding an OB polypeptide under conditions that provide for expression of the polypeptide *in vivo*, said polypeptide, capable of modulating body weight, comprising the amino acid sequences set out in amino acids 22-167 of SEQ ID NOS: 2 or 4 or in amino acids 22-166 of SEQ ID NOS: 5 or 6 wherein said polypeptide has an N-terminal amino acid sequence selected from the group consisting of:

- (a) SEQ ID NO: 38;
- (b) SEQ ID NO: 98;
- (a) SEQ ID NO: 26;
- (b) SEQ ID NO: 27;
- (c) SEQ ID NO: 28;
- (d) SEQ ID NO: 99; and
- (e) glycine-serine-proline.

168. A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding an OB polypeptide analog under conditions that provide for expression of the polypeptide analog *in vivo*, said analog, capable of modulating body weight, comprising amino acids 22-167 of SEQ ID NOS: 2 or 4, wherein one or more amino acids selected from the group consisting of amino acids 53, 56, 71, 85, 89, 92, 95, 98, 110, 118, 121, 122, 126, 127, 128, 129, 132, 139, 157, 159, 163, and 166 is substituted with another amino acid and wherein said analog has an N-terminal amino acid or amino acid sequence selected from the group consisting of:

- (a) methionine;
- (b) SEQ ID NO: 38;
- (c) SEQ ID NO: 98;
- (d) SEQ ID NO: 26;
- (e) SEQ ID NO: 27;
- (f) SEQ ID NO: 28;

(g) SEQ ID NO: 99; and
(h) glycine-serine-proline.

169. A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding an OB polypeptide analog under conditions that provide for expression of the polypeptide analog *in vivo*, said analog, capable of modulating body weight, comprising an amino acid sequence of SEQ ID NOS: 2 or 4, wherein said analog is a truncated analog selected from the group consisting of polypeptides wherein:

(a) one or more residues at positions 121 to 128 are deleted;
(b) residues 1-116 are deleted;
(c) residues 1-21 and 54 to 167 are deleted;
(d) residues 1-60 and 117 to 167 are deleted;
(e) residues 1-60 are deleted;
(f) residues 1-53 are deleted;
(g) an analog of subpart (a) wherein residues 1-21 are deleted; and
(h) an analog of any of subparts (a) through (g) having an N-terminal amino acid or amino acid sequence selected from the group consisting of:

(1) methionine,
(2) SEQ ID NO: 38,
(3) SEQ ID NO: 98,
(4) SEQ ID NO: 26,
(5) SEQ ID NO: 27,
(6) SEQ ID NO: 28,
(7) SEQ ID NO: 99, and
(8) glycine-serine-proline.

170. A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding an OB polypeptide analog under conditions that provide for expression of the polypeptide analog *in vivo*, said analog,

capable of modulating body weight, comprising amino acids 22-166 of SEQ ID NOS: 5 or 6 wherein said analog is selected from the group consisting of polypeptides wherein:

- (a) the serine residue at position 52 is substituted with glycine, alanine, valine, cysteine, methionine, or threonine;
- (b) the serine residue at position 97 is substituted with glycine, alanine, valine, cysteine, methionine, or threonine; and
- (c) the arginine residue at position number 91 is substituted with asparagine, lysine, histidine, glutamine, glutamic acid, aspartic acid, serine, threonine, methionine, or cysteine.

171. A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding an OB polypeptide analog under conditions that provide for expression of the polypeptide analog *in vivo*, said analog, capable of modulating body weight, comprising an amino acid sequence of SEQ ID NOS: 5 or 6, wherein said analog is selected from the group consisting of polypeptides wherein:

- (a) one or more aspartic acid residues is substituted with glutamic acid;
- (b) one or more isoleucine residues is substituted with leucine;
- (c) one or more glycine or valine residues is substituted with alanine;
- (d) one or more arginine residues is substituted with histidine;
- (e) one or more tyrosine or phenylalanine residues is substituted with tryptophan;
- (f) one or more of residues 120 through 127 is substituted with glycine or alanine; and
- (g) one or more residues at positions 53 through 59 or 117 through 165 is substituted with lysine, glutamic acid, cysteine, or proline.

172. A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding an OB polypeptide analog under conditions that provide for expression of the polypeptide analog *in vivo*, said analog, capable of modulating body weight, comprising an amino acid sequence of SEQ ID NOS: 5 or 6, wherein said analog is a truncated analog selected from the group consisting of polypeptides

wherein:

- (a) one or more residues at positions 120 through 127 are deleted;
- (b) residues 1-115 are deleted;
- (c) residues 1-21 and 53 to 166 are deleted;
- (d) residues 1-59 and 116 to 166 are deleted;
- (e) residues 1-59 are deleted;
- (f) residues 1-52 are deleted;
- (g) an analog of subpart (a) wherein residues 1-21 are deleted; and
- (h) an analog of any of subparts (a) through (g) having an N-terminal amino

acid or amino acid sequence selected from the group consisting of:

- (1) methionine,
- (2) SEQ ID NO: 38,
- (3) SEQ ID NO: 98,
- (4) SEQ ID NO: 26,
- (5) SEQ ID NO: 27,
- (6) SEQ ID NO: 28,
- (7) SEQ ID NO: 99, and
- (8) glycine-serine-proline.

173. A method for modifying the body weight of a mammal comprising administering to the mammal a vector comprising a nucleic acid molecule encoding an OB polypeptide analog under conditions that provide for expression of the polypeptide analog *in vivo*, said analog, capable of modulating body weight, comprising amino acids 22-166 of SEQ ID NOS: 5 or 6, wherein one or more amino acids selected from the group consisting of amino acids 52, 55, 70, 84, 88, 91, 94, 97, 109, 117, 120, 121, 125, 126, 127, 128, 131, 138, 156, 158, 162, and 165 is substituted with another amino acid and wherein said analog has an N-terminal amino acid or amino acid sequence selected from the group consisting of:

- (a) methionine;
- (b) SEQ ID NO: 38;